

WHAT IS CLAIMED IS:

1. A method of treating cardiac disease in a mammal comprising administering to said mammal an effective amount of a compound or agent that blocks or otherwise inhibits Mst1 or the Mst1 pathway.
2. The method of Claim 1 wherein said compound or agent is an Mst1 inhibitor.
3. The method of Claim 1 wherein the Mst1 inhibitor is selected from the group of a dominant negative mutant of Mst1, an inhibitor of caspase, an inhibitor of apoptosis, antisense oligonucleotide complementary to Mst1, siRNA to Mst1 and a ribozyme directed against Mst1.
4. The method of Claim 3, wherein said Mst1 inhibitor is selected from the group of inhibitors against Caspase 3, Chelerythrine and Calyculin A.
5. The method of Claim 1 wherein said compound or agent inhibits a protein that phosphorylates Mst1, cleaves Mst1 to generate active Mst1, or activates an Mst1 phosphatase.
6. The method of Claim 1 wherein said cardiac disease is selected from the group of congestive heart failure, cardiomyopathy, including ischemic and nonischemic cardiomyopathy, coronary artery disease, arrhythmias, fibrosis of the heart, valve defects, atherosclerosis, and instances where facilitation of enhanced heart function or maintenance of cardiac myocytes is desired.
7. The method of Claim 1 wherein said mammal is a human.

8. A method of modulating cardiac myocyte apoptosis in a mammal comprising administering to said mammal an effective amount of a compound or agent that blocks or otherwise inhibits Mst1 or the Mst1 pathway.
9. The method of Claim 8 wherein the Mst1 inhibitor is selected from the group of a dominant negative mutant of Mst1, an inhibitor of caspase, an inhibitor of apoptosis, antisense oligonucleotide complementary to Mst1, siRNA to Mst1 and a ribozyme directed against Mst1.
10. A method for reducing cardiomyopathy in a mammal comprising administering to said mammal an effective amount of an Mst1 inhibitor.
11. A method for treating cardiac disease in a mammal comprising administering to said mammal an effective amount of a Mst1 inhibitor in combination with one or more other compound for treatment of cardiac disease or of atherosclerosis.
12. The method of Claim 11 wherein said one or more other compound selected from the group of a beta-blocker, nitrate, calcium channel antagonists, angiotensin-converting enzyme (ACE) inhibitors, an anti-platelet drug, diuretics, digoxin and antilipemic agents, agents which alter cholesterol or lipid metabolism.
13. A method for reducing the risk of cardiomyopathy or cardiac dysfunction in a mammal wherein said mammal has suffered a myocardial infarct or other coronary event wherein blood flow to the heart is reduced comprising administering to said mammal an effective amount of an Mst1 inhibitor or Mst1 pathway inhibitor.
14. The method of Claim 13 wherein the Mst1 inhibitor is selected from the group of a dominant negative mutant of Mst1, an inhibitor of caspase, an inhibitor of apoptosis,

antisense oligonucleotide complementary to Mst1, siRNA to Mst1 and a ribozyme directed against Mst1.

15. A method of cardioprotection, wherein an inhibitor of Mst1 is administered in conjunction with or following therapy with a compound or drug which is cardiotoxic.

16. The method of Claim 15 wherein said compound is a chemotherapeutic agent, particularly an anti-cancer or anti-tumor agent.

17. The method of Claim 16 wherein said chemotherapeutic agent is doxorubicin.

18. A method of screening for compounds which modulate cardiac myocyte apoptosis comprising selecting compounds which inhibit Mst1 or the Mst1 pathway and performing assays with said compounds to determine the amount or extent of cardiac myocyte apoptosis.

19. The method of Claim 18 wherein selecting compounds that modulate Mst1 or the Mst1 pathway comprises incubating Mst1 with a candidate compound, and conducting phosphorylation assays wherein a compound's ability to block phosphorylation of Mst1 or by Mst1 or enhance dephosphorylation of Mst1 is determined.

20. The method of Claim 18 wherein selecting compounds that modulate Mst1 or the Mst1 pathway comprises incubating Mst1 with a candidate compound, and conducting assays wherein a compound's ability to block the activity of a molecule downstream of Mst1 or which is modulated or activated by Mst1 or upon Mst1 phosphorylation or cleavage is determined.

21. The method of Claim 20 wherein the molecule downstream of Mst1 is selected from the group of caspase 3, caspase 5, MBP, MAPK and JNK.

22. A composition for modulating cardiac myocyte apoptosis comprising an Mst1 inhibitor.

23. The composition of Claim 22 wherein said Mst1 inhibitor inhibits a protein that phosphorylates Mst1, activates an Mst1 phosphatase, inhibits a protein that cleaves and/or activates Mst1, is an antagonist of Mst1, or is a dominant negative form Mst1.

24. A pharmaceutical composition for treatment or amelioration of cardiac disease in a mammal comprising a therapeutically effective amount of one or more Mst1 inhibitor and a pharmaceutically acceptable carrier.

25. A pharmaceutical composition for treatment or amelioration of cardiac disease in a mammal comprising a therapeutically effective amount of a combination of one or more Mst1 inhibitor and one or more other compounds for the treatment of cardiac disease or atherosclerosis and a pharmaceutically acceptable carrier.

26. The pharmaceutical composition of Claim 25 wherein the one or more other compounds for the treatment of cardiac disease or atherosclerosis are selected from the group of a beta-blocker, nitrate, calcium channel antagonists, angiotensin-converting enzyme (ACE) inhibitors, an anti-platelet drug, diuretics, digoxin and antilipemic agents, agents which alter cholesterol or lipid metabolism.

27. The pharmaceutical composition of Claim 25 or 26 wherein the cardiac disease is selected from the group of congestive heart failure, cardiomyopathy, including ischemic and nonischemic cardiomyopathy, coronary artery disease, arrhythmias, fibrosis of the

heart, valve defects, atherosclerosis, and instances where facilitation of enhanced heart function or maintenance of cardiac myocytes is desired.

28. An assay system for screening of potential compounds or agents effective to modulate Mst1 activity of target mammalian cells by interrupting or potentiating the Mst1 or Mst1 pathway wherein the test compound or agent is administered to a cellular sample to determine its effect upon the kinase activity, cleavage status or phosphorylation status of Mst1, by comparison with a control.

29. An assay system for screening compounds or agents for the ability to modulate the activity of Mst1, comprising:

- A. culturing an observable cellular test colony inoculated with a compound or agent;
- B. harvesting a supernatant from said cellular test colony; and
- C. examining said supernatant for the activity of said Mst1 wherein an increase or a decrease in the activity of said Mst1 indicates the ability of a drug to modulate the activity of said Mst1.

30. A method for treating or ameliorating cardiac disease in a mammal comprising administering to said mammal a nucleic acid or vector capable of encoding a dominant negative form of Mst1 such that said dominant negative form of Mst1 is expressed in the heart of said mammal.

31. The method of Claim 30 wherein the dominant negative form is expressed in cardiac myocytes and wherein the dominant negative form of Mst1 antagonizes the endogenous form of Mst1 such that Mst1 is inhibited.

32. An animal model of cardiac disease, including cardiac myopathy, comprising a transgenic animal wherein Mst1 expression or activity is enhanced.

33. The animal model of Claim 32 wherein the transgenic animal is selected from the group of rats, mice, pigs, chicken, cows, monkeys, rabbits, sheep and dogs.